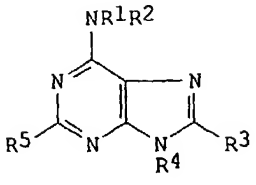
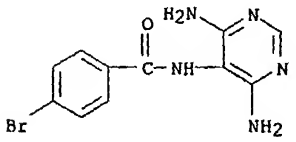


I

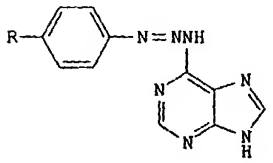
AB A method and compn. is disclosed for detg. the viability of tissue in a region of an organism having a vascular circulatory system that supplies blood to the region; the method includes: (1) dilating the above vascular circulation system by introducing adenosine or an adenosine agonist into the vascular circulation system to increase the blood flow into the region; (2) introducing a blood flow marking medium into the region; (3) alleviating the non-dilating effects of adenosine or the adenosine agonist by introducing an A1 adenosine receptor antagonist into the vascular circulatory system; and (4) detg. the amt. of marking medium in the region. The compns. of the invention include I [R1 = H, R2; R2 = endo-2-norbornyl, cyclopentyl; R3 = H, halo, amine, carboxy, C1-10 alkyl, etc.; R4 = benzyl, Ph, (O-substituted) C1-4 alkyl (e.g. ethers, alcs.); R5 = H, OH, sulfonate, halo, C1-6 (cyclo)alkoxy]. The method and compn. of the invention are useful in thallium-201 scintigraphy, and decrease side effects through alleviating the A1 effects of adenosine as an A1 antagonist while maintaining the A2 vasodilation activity of adenosine. Prepn. of selected I is included, and various I were assayed in A1 and A2 test systems.

L3 ANSWER 49 OF 70 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1981:406196 CAPLUS
DN 95:6196
TI Reactions of benzenediazonium ions with adenine and its derivatives
AU Chin, Anton; Hung, Ming-Hong; Stock, Leon M.

CS Dep. Chem., Univ. Chicago, Chicago, IL, 60637, USA
SO Journal of Organic Chemistry (1981), 46(11), 2203-7
CODEN: JOCEAH; ISSN: 0022-3263
DT Journal
LA English
IT **77071-06-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 77071-06-8 CAPLUS
CN Benzamide, 4-bromo-N-(4,6-diamino-5-pyrimidinyl)- (9CI) (CA INDEX NAME)



GI



I

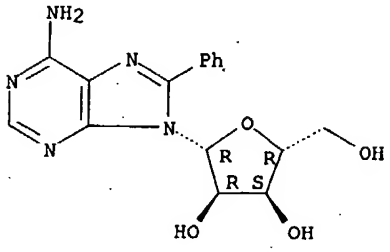
AB Adenine, adenosine and 5'-adenylic acid react readily with benzenediazonium ion and its derivs. at pH 8-11 to yield derivs. of (E)-6-(3-phenyl-2-triazen-1-yl)purine, e.g., I (R = H, Me, Br, SO3H). The triazenes decomp. in basic aq. soln. at 60-90.degree. to produce 8-aryladenines, apparently via intermol. processes. For adenosine and 5'-adenylic acid, the ribose residues are cleaved during this process. Both p-RC6H4N2+ and p-RC6H4.bul. can be intercepted during the reaction. Consequently, the phenylation reaction may be confidently formulated as an intermol. free-radical substitution.

L3 ANSWER 62 OF 147. CAPLUS COPYRIGHT 2003 ACS on STN
AN 1994:645130 CAPLUS
DN 121:245130
TI Selective Inhibition of Trypanosomal Glyceraldehyde-3-phosphate Dehydrogenase by Protein Structure-Based Design: Toward New Drugs for the Treatment of Sleeping Sickness
AU Verlinde, Christophe L. M. J.; Callens, Mia; Van Calenbergh, Serge; Van Aerschot, Arthur; Herdewijn, Piet; Hannaert, Veronique; Michels, Paul A. M.; Opperdoes, Fred R.; Hol, Wim G. J.
CS School of Medicine, University of Washington, Seattle, WA, 98195, USA
SO Journal of Medicinal Chemistry (1994), 37(21), 3605-13
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
IT 73340-78-0P, 8-Phenyladenosine 158555-06-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(protein structure-based design of selective inhibition of glyceraldehyde phosphate dehydrogenase complexes of humans and Trypanosoma brucei in treatment of sleeping sickness)

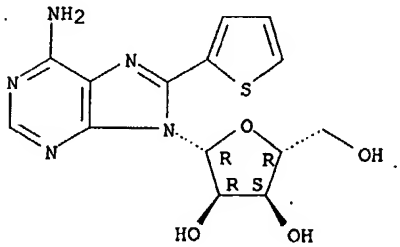
RN 73340-78-0 CAPLUS
CN Adenosine, 8-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 158555-06-7 CAPLUS
CN Adenosine, 8-(2-thienyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB Within the framework of a project aimed at rational design of drugs against diseases caused by trypanosomes and related hemoflagellate parasites, selective inhibitors of trypanosomal glycolysis were designed, synthesized, and tested. The design was based upon the crystallog. detd. structures of the NAD:glyceraldehyde-3-phosphate dehydrogenase complexes of humans and Trypanosoma brucei, the causative agent of sleeping sickness. After one design cycle, using the adenosine part of the NAD cofactor as a lead, the following encouraging results were obtained: (1) a 2-Me substitution, targeted at a small pocket near Val 36, improves inhibition of the parasite enzyme 12.5-fold; (2) an 8-(thien-2-yl) substitution, aimed at Leu 112 of the parasite enzyme, where the equiv. residue in the mammalian enzyme is Val 100, results in a 167-fold better inhibition of the trypanosomal enzyme, while the inhibition of the human enzyme is improved only 13-fold; (3) exploitation of a "selectivity cleft" created by a unique backbone conformation in the trypanosomal enzyme near the adenosine ribose yields a considerable improvement in selectivity: 2'-deoxy-2'-(3-methoxybenzamido)adenosine e inhibits the human enzyme only marginally but enhances inhibition of the parasite enzyme 45-fold when [illegible] adenosine. The designed inhibitors are not only better